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Molecular Epidemiology of *Neisseria meningitidis* Isolates from an Outbreak of Meningococcal Disease among Men Who Have Sex with Men, Chicago, Illinois, 2003▽

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We characterized five *Neisseria meningitidis* serogroup C isolates from a Chicago outbreak of meningococcal disease that occurred in 2003 among a community of men who have sex with men. Isolates from this outbreak were identical to each other but distinct from the clone that caused a similar outbreak in Canada in 2001.

In 2003, an outbreak of invasive meningococcal disease occurred in a Chicago community of men who have sex with men (MSM). To our knowledge, this was the first reported outbreak of meningococcal disease among MSM in the United States. In 2001, a similar outbreak of invasive meningococcal disease occurred among MSM in Toronto. The Toronto outbreak was caused by a unique clone of *Neisseria meningitidis* serogroup C (NmenC) of phenotype C:NT:P1.2, and a subsequent investigation identified bathhouses as the potential venue for transmission of the organism (11). We characterized the Chicago NmenC isolates to determine if the same clone accounted for the only two reported outbreaks of meningococcal disease among MSM.

In October 2003, the Chicago Department of Public Health (CDPH) received reports of six cases of invasive meningococcal disease among adult men aged 27 to 42 years. The patients had onset of illness between 6 and 15 October. All patients presented with septicemia and petechial or purpuric rash; three patients died. The human immunodeficiency virus status of the patients is unknown. NmenC was isolated from the blood of five patients. The sixth case was diagnosed as serogroup C meningococcal disease on the basis of a PCR assay of cerebrospinal fluid and immunohistochemical staining of fixed tissues.

An epidemiologic investigation revealed that all cases occurred among MSM. All six patients patronized several MSM-oriented social venues on Chicago's north side during the 10 days prior to the onset of illness. Four of the patients had visited the same bar prior to onset, two patients had reportedly kissed, and another two patients may have had anonymous sexual contact with each other.

In response to the outbreak, CDPH distributed health alert notices and fact sheets to health care providers known to serve significant proportions of the MSM community. To prevent additional cases, CDPH conducted an 8-day vaccination and prophylaxis campaign focused on patrons of MSM-oriented venues in Chicago. Campaign efforts at six sites in Chicago administered 14,267 doses of the quadrivalent meningococcal polysaccharide vaccine. Enhanced surveillance identified no additional cases.

Blood culture isolates from five patients were identified as NmenC by standard microbiological identification methods and slide agglutination at the local hospital laboratories and the Illinois Department of Public Health. The five isolates from the Chicago outbreak and one representative serogroup C reference strain from the 2001 Toronto outbreak were provided to the Centers for Disease Control and Prevention (CDC) for confirmation and molecular characterization, including multilocus sequence typing (MLST), *fumC* gene sequencing, DNA sequencing of the variable regions (VR) of the *porA* and *porB* genes, 16S rRNA gene sequencing, and pulsed-field gel electrophoresis (PFGE). MLST sequences were submitted to the *Neisseria* MLST website (http://pubmlst.org/neisseria) (5) and were assigned sequence types. The *fumC* gene was examined for the presence of a G-to-A point mutation at position 640 to determine if the isolates were of the enzyme type 15 (ET-15) lineage, which is characterized by this mutation (12). The predicted amino acid sequences from *porA* and *porB* gene VR were edited and compared with sequences available in the *N. meningitidis* PorA and PorB typing database (http://neisseria.org) (8, 9). 16S rRNA gene sequencing and pulsed-field gel electrophoresis (PFGE) analysis of NheI restriction-digested DNA was performed as previously described (10, 7). 16S rRNA gene sequences and PFGE pattern profiles were compared to sequences and profiles contained in the CDC databases composed of a convenience sample of 600 invasive and carriage isolates collected from outbreak and sporadic cases in the United States from 1989 to 2006. The PFGE pattern profiles from the outbreak isolates were also compared to the pattern profiles for the only other NmenC isolates from culture-confirmed invasive meningococcal disease cases identified in Chicago in 2003 and 2004.

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TABLE 1. Characteristics of the *N. meningitidis* isolates recovered from the Chicago and Toronto outbreaks

Outbreak location, yr	Serogroup	MLST	MLEE[e] type	$fumC_{640}$ point mutation	*porA* VR type	*porB* VR type	16S rRNA gene sequence type	PFGE type
Chicago, 2003	C	ST-11	ND[d]	G → A	P1.5-1,10-8	I.1, V.1, VI.1, VII.1	166	H46N06.0183
Toronto, 2001[a]	C	ST-11	ET-15	G → A	P1.5,2	I.1, V.1, VI.1, VII.1[b]	13	H46N06.0214[c]

[a] Toronto data are from Tsang et al. (11), except for the MLST, the *porA* VR type, the 16S rRNA gene sequence type, and the PFGE pattern designation.
[b] The *porB* VR type of the Toronto isolate is most similar to I.1, V.1, VI.1, VII.1; however, this designation does not denote the nucleotide substitution in VR3 of the Toronto isolate (11).
[c] PFGE pattern H46N06.0214 was <85% similar to H46N06.0183 and differed by more than five bands (7).
[d] ND, not done.
[e] MLEE, multilocus enzyme electrophoresis.

Molecular characterization determined that the five Chicago NmenC isolates were indistinguishable from each other but distinct from the Toronto clone (Table 1). All of the isolates were of MLST sequence type 11 (ST-11) and contained the $fumC_{640}$ A point mutation characteristic of ET-15 strains. Sequencing of *porA* VR1 and VR2 demonstrated that the Chicago isolates were of type P1.5-1,10-8, whereas the Toronto outbreak isolate was of type P1.5,2. VR sequencing of the *porB* genes indicated that the Chicago isolates were of VR type I.1, V.1, VI.1, VII.1. By the nomenclature of Sacchi et al. (10), this *porB* VR type would be C, E_b, 2a, C. Tsang described the *porB* VR type of the Toronto outbreak strain with the nucleotide substitution in VR3 as C, E_b, 2a(a), C (11). The *porB* VR type described by Tsang et al. is currently not in the *Neisseria*.org PorB typing database but is most similar to I.1, V.1, VI.1, VII.1.

16S rRNA gene sequencing showed that the Chicago isolates were identical, type 166. This 16S type was novel in the United States and not previously found in any of the 119 serogroup C sequences in the database at the CDC. 16S type 166 differs by a single change from 16S types 12 and 13 that were previously described as the predominant 16S types in serogroup C outbreaks in Arizona, New Mexico, Texas, California, and Toronto (10).

PFGE analysis revealed that all of the Chicago isolates produced the same pattern, H46N06.0183. This PFGE pattern was <85% similar to the patterns of all of the culture-confirmed invasive serogroup C cases that occurred in Chicago from 2003 to 2004 and matched only 1 (0.3%) of the 363 serogroup C patterns contained in the CDC database. The serogroup C isolate with the same pattern was collected in Maryland in 2002. The PFGE pattern produced by the Toronto reference strain (H46N06.0214) was distinct (<85% similar) from that of the Chicago strain and differed by more than five bands.

There are several similarities between this outbreak and the previously described meningococcal disease outbreak that occurred in Toronto in 2001. Both outbreaks occurred in MSM communities and were characterized by high case fatality rates (i.e., three of six patients in Chicago and two of six patients in Toronto). In addition, both outbreaks were caused by ET-15 NmenC, ST-11 strains. Isolates of the ST-11 complex are known to cause a high proportion of invasive disease relative to asymptomatic carriage and have been linked to a number of outbreaks in the United States and internationally (5, 10, 13). Among ST-11 strains, the Chicago strain is distinct, as shown by comparisons of the16S and PFGE types with other U.S. isolates. These findings support the hypothesis that serogroup C outbreaks are precipitated by the introduction of a meningococcal strain that differs, even slightly, from strains previously circulating in the population.

Despite the similarities in outbreak characteristics and *N. meningitidis* sequence types, the Chicago and Toronto outbreaks were caused by distinct meningococcal clones. The five isolates from the Chicago outbreak were indistinguishable by extensive molecular characterization but differed from the Toronto isolate by *porA* and *porB* VR type, 16S rRNA gene sequence type, and PFGE pattern type. These data suggest that factors other than a common meningococcal clone may have contributed to the outbreaks in these two MSM communities. Meningococcal disease outbreaks have been associated with schools, bars, and other social networks or institutions (1–4, 6, 14). Further study is needed to evaluate whether practices common in MSM communities may be risk factors for the transmission of invasive meningococcal disease among MSM.

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